Advances in the Treatment of Pelvic Floor Dysfunction

Highlights from the 23rd Annual Scientific Meeting of the American Urogynecologic Society, October 17-19, 2002, San Francisco, CA

[*Rev Urol.* 2003;5(4):235-240]

© *2003 MedReviews, LLC*

Key words: Urinary incontinence • Overactive bladder • Pelvic organ prolapse • Interstitial cystitis • Magnetic resonance imaging • Total colpocleisis • Renal transplantation • Tension-free vaginal tape • Duloxetine • Oxybutynin • Resiniferatoxin • Tolterodine • Uryx

On October 17-19, 2002, leading urogynecologists from around North America gathered in San Francisco for the 23rd Annual Scientific Meeting of the American Urogynecologic Society (AUGS). The principal mission of this meeting was to bring together urogynecologists to discuss the latest developments in the area of pelvic floor dysfunction. There are 3 good reasons why the urologic community should be aware of this meeting.

First, urinary incontinence and pelvic floor prolapse are areas of importance to both urologists and urogynecologists. Although there is collaboration between these specialists in some medical centers, in others there is competition. We believe that a lack of communication and understanding between the 2 specialties inhibits productive collaboration.

Second, the AUGS is a superbly organized society that maintains the feeling of a close-knit community. The AUGS provides urologists with an opportunity to learn how to organize an exceptional society that truly cares about its members.

Third, urologists will be interested to know that the topics discussed at the AUGS meeting were broad-based and included basic research,

Reviewed by Tracy W. Cannon, MD, Nancy Howden, MD, Macrina Xavier, BS, and Michael B. Chancellor, MD, University of Pittsburgh School of Medicine, Pittsburgh, PA

clinical trials, and epidemiology, as well as specific topics such as the treatment of prolapse, stress urinary incontinence (SUI), and overactive bladder (OAB). Together, urologists and urogynecologists can work toward the common goal of treating incontinence.

Following are summaries of some of the many noteworthy presentations made at the 23rd Annual Meeting of the AUGS.

Is There an Injectable Urethral Bulking Agent That Can Compete With Collagen?

Karram[1] presented the results of a study evaluating the safety and efficacy of the Uryx® urethral bulking agent (Genyx Medical, Aliso Viejo, Calif) for the treatment of female urinary incontinence and comparing this device with the Contigen® Bard Collagen Implant (C. R. Bard, Murray Hill, NJ). Uryx is an injectable solution of ethylene vinyl alcohol copolymer dissolved in a dimethyl sulfoxide (DMSO) carrier. On contact with an aqueous environment, such as the submucosal tissues of the urethra, the DMSO solvent diffuses away, resulting in precipitation of the polymer, which forms a cohesive, spongy mass that creates a bulking effect. The low viscosity of Uryx enables easy hand injection through a fine (25-g) needle. The precipitated polymer mass volume is essentially equivalent to that of the injected solution and does not change over time.

A total of 210 women with genuine SUI were prospectively treated with either Uryx or Contigen, with a randomization ratio of 2:1 in favor of Uryx. The average patient age for both groups was 60 ± 13 years. Historical symptom duration was 9.7 ± 8.8 years for the Uryx group and 9.7 ± 8.6 years for the Contigen group. Patients were assessed posttreatment with objective urodynamic testing and subjective patient questionnaires. Pad weights and symptom scores were presented on all available patients at 6 months posttreatment.

Mean total volumes injected per patient were 4.2 mL with Uryx and 7.0 mL with Contigen. Six-month pad weight success rates were "dry" in 63% (24/38) of the subjects who received Uryx and 45% (9/20) of those who received Contigen; they were "improved" in 13% (5/38) of the subjects who received Uryx and 30% (6/20) of those who received Contigen. This calculated to overall dry/improved rates of 76% with Uryx and 75% with Contigen. At 6 months, symptom scores indicated improvement in 67% (26/39) of the patients who received Uryx and 62% (13/21) of those who received Contigen. The majority of adverse effects occurred early (within 28 days of treatment) and resolved rapidly. The 2 most common complications in both treatment groups were urge (Uryx, 22%; Contigen, 21%) and dysuria (Uryx, 16%; Contigen, 15%). No serious unanticipated events were reported in either treatment group.

The physical characteristics of the Uryx bulking agent allow delivery of the desired volume through a small-gauge needle. The injected volume remains fixed, and a durable, cohesive mass is formed. These properties appear to offer promising clinical advantages. Overall, the data to date indicate no significant clinical or safety issues when Uryx is compared directly with Contigen.

OAB and Sexual Function

One topic related to OAB that has received little attention until now is the possible relationship between OAB and female sexual dysfunction. Sand and colleagues[2] presented results from an interesting (industry-sponsored) study in which women received extended-release oxybutynin for OAB and were evaluated for assessment of the impact of OAB on their sexual function. A total of 1136 women were studied in a 12-week, open-label evaluation. The women had urge incontinence and other symptoms of OAB and received titrated doses of 5 mg to 30 mg of oxybutynin. Patients completed urinary incontinence and sexual function diaries.

Oxybutynin therapy resulted in a decrease in the negative effects of OAB on female sexual function.

Results showed that OAB often or always negatively impacted sexual activities in up to 25% of subjects. The impact of OAB on sexual function was more severe among women who had more than 14 weekly urge incontinence episodes and in those younger than 40 years. After 12 weeks of controlled-release oxybutynin therapy, a substantial decrease in the negative effects of OAB on sexual activities and function was observed.

The authors concluded that OAB negatively affects female sexual function and that this negative effect seems to be more pronounced with increasing severity of the condition and in younger women. Oxybutynin therapy resulted in a decrease in the negative effects of OAB on female sexual function.

Treating Advanced Pelvic Organ Prolapse

Urologists should be aware of an operative procedure that is helpful for the treatment of severe pelvic prolapse in select elderly or medically fragile women who no longer desire to maintain sexual function. Total

colpocleisis involves the complete excision of the vaginal epithelium, pursestring suture reduction of the prolapsed viscera, and plication of the puborectalis and pubococcygeus muscles. von Pechmann and colleagues[3] reported results of a retrospective study describing the nature and clinical results of their method of colpocleisis over a 12-year period.

Ninety-two women, aged 56 to 92 years (mean, 78 ± 5.8 years), with uterovaginal or vaginal vault eversion underwent total colpocleisis in conjunction with other procedures. Twenty-eight women had previously undergone a total of 42 surgical repairs for prolapse. Thirty-seven patients (40%) underwent vaginal hysterectomy concurrently with colpocleisis. Ninety patients (98%) underwent an adjunctive procedure at the time of colpocleisis, including 31 pubourethral ligament plications, 7 needle suspensions of the bladder neck, and 52 suburethral sling procedures. Median office follow-up time was 12 months, and median telephone follow-up time was 24 months (range, 13-161 months).

The objective cure rate was 98% (90/92). Of the 2 patients who presented postoperatively with prolapse reaching the hymen, 1 was cured after reoperation and the other was asymptomatic. Of 62 patients directly contacted by telephone, 56 (90.3%) reported being satisfied or very satisfied with the way the operation cured their prolapse. Two (3.2%) of the 62 patients expressed regret about the loss of coital ability, but only 1 of the 2 (1.6%) stated that she would not again choose to have the surgery.

Total colpocleisis with levator plication is a vaginal operation for advanced pelvic organ prolapse that has an excellent success rate. The operation can be performed in concurrence with other procedures, including hysterectomy. The majority of patients express satisfaction with this procedure.

Effect of Tension-Free Vaginal Tape on Voiding

Lukacz and colleagues[4] conducted a study to determine whether the tension-free vaginal tape (TVT) sling procedure (Ethicon, Sommerville, NJ) altered micturition. This prospective cohort study evaluated 65 consecutive patients who underwent the TVT sling procedure for the treatment of urodynamic SUI. Free-flow voiding studies and voiding cystometry were performed preoperatively and 1 year postoperatively.

The TVT sling significantly decreased the maximum flow rate without a significant effect on detrusor pressure.

Forty-one patients (69%) were available for follow-up at 1 year. The mean age of these patients was 62 years (range, 31-82 years). Ten patients (24%) had previous anti-incontinence operations. Twenty-nine patients (71%) had the TVT procedure only; the remainder (29%) underwent additional reconstructive pelvic surgery at the time of the TVT procedure. Fourteen (34%) of the 41 patients had incomplete emptying or urinary retention necessitating transurethral bladder drainage or intermittent catheterization (median duration, 3.5 days; range, 1-53 days). Three subjects (7%) required sling release.

The TVT sling significantly decreased the maximum flow rate without a significant effect on detrusor pressure. There was no correlation between postoperative urinary retention and low flow rates at 1 year. The procedure does not seem to cause significant obstruction given the normal detrusor pressures; however, longer follow-up is necessary to evaluate possible delayed effects on detrusor pressures.

Duloxetine for Mixed SUI/OAB Symptoms

Investigators from the Duloxetine SUI Study Group presented results of a study comparing women with pure SUI symptoms with those with mixed SUI/OAB symptoms with respect to incontinence severity and treatment response to duloxetine.[5] In previous treatment trials, duloxetine, a dual serotonin and norepinephrine reuptake inhibitor, has been demonstrated to significantly improve both the frequency of incontinence episodes and patient quality of life.[6,7]

A total of 683 women with predominant symptoms of SUI were enrolled. Assessment variables included incontinence episode frequency, the Incontinence Quality of Life Questionnaire (I-QOL), and the Patient Global Impression of Severity Scale (baseline only). SUI was defined according to a clinical algorithm with a sensitivity of 92% for urodynamic stress incontinence. Urge symptoms were identified with 3 urge-related I-QOL questions previously confirmed to be significantly associated with urodynamic detrusor overactivity.

Forty-three percent of subjects had mixed symptoms before treatment. Women with mixed symptoms had significantly more daily voids and more voids associated with urgency than did women with pure SUI. Mixed-symptom subjects also had more severe urge incontinence at baseline than those with SUI only.

After treatment, 57% of the subjects who had mixed symptoms at baseline reverted to SUI only. Subjects with persistent mixed symptoms had

more severe urge incontinence post-treatment than those in whom these symptoms resolved. Both symptom groups had significant decreases in incontinence episode frequency with duloxetine, 80 mg/d, compared with placebo ($P < .001$).

Mixed symptoms were associated with more severe urge incontinence; as urge incontinence severity improved, mixed symptoms reverted to pure symptoms.

Thus, in a population of women with predominant symptoms of SUI, duloxetine demonstrated equal efficacy for women with mixed SUI/OAB symptoms and those with pure SUI. Mixed symptoms were associated with more severe urge incontinence; as urge incontinence severity improved, mixed symptoms reverted to pure symptoms.

Transdermal Versus Oral Oxybutynin for OAB

Neimark and colleagues[8] evaluated changes in cystometrogram (CMG) parameters in patients receiving transdermal oxybutynin or immediate-release oral oxybutynin. Patients with OAB were enrolled in a randomized, double-blind study evaluating the efficacy and adverse effects of oral and transdermal oxybutynin. Differences in CMG parameters from baseline and at 6 weeks of treatment were compared between groups. Results showed that transdermal oxybutynin significantly increased bladder volume at first involuntary detrusor contraction but did not affect any other CMG parameter compared with immediate-release oral oxybutynin.

Transdermal Oxybutynin Versus Controlled-Release Tolterodine for OAB

Dmochowski and colleagues[9] compared transdermal oxybutynin with controlled-release tolterodine for the treatment of OAB. A total of 361 patients with OAB underwent treatment washout; baseline evaluation via a voiding diary; and subsequent randomized, blinded treatment with controlled-release tolterodine (4 mg qd), transdermal oxybutynin (3.9 mg/d twice weekly), or matched placebo for 3 months.

Complete continence was achieved in 38% of the subjects who received controlled-release tolterodine and 40% of those who received transdermal oxybutynin. Dry mouth was more common in those who received controlled-release tolterodine (7.3%) than in those who received transdermal oxybutynin (4.1%). Although there was no statistical difference in efficacy between the 2 treatment groups, the incidence of dry mouth was significantly higher in the subjects who received controlled-release tolterodine than in those who received placebo.

Renal Transplantation and Urinary Incontinence

We thought it notable that urogynecologists are becoming interested in renal transplantation. Heit and colleagues[10] examined the prevalence, type, and severity of urinary incontinence and its effect on activities of daily living in renal transplant recipients.

All female patients attending a renal transplantation clinic were asked to participate in a survey in which continence status, type of incontinence, severity index, and effect of incontinence on activities of daily living were ascertained by standardized questions validated in prior incontinence studies. All patients were asked to complete a 3-day bladder diary. Demographic and clinical data from posttransplant incontinent and continent patients were compared.

Of 123 female transplant recipients, 100 completed the survey, for a response rate of 81.3%. The prevalence of urinary incontinence in female transplant recipients was 28%. Stress, urge, and mixed incontinence were reported in 32.1%, 25.0%, and 42.9% of cases, respectively.

A history of urinary incontinence before renal failure was not predictive of posttransplant incontinence. Only 6 (21.4%) of 28 incontinent transplant recipients reported a history of incontinence before renal failure. Age, race, body mass index, vaginal parity, tobacco use, and creatinine levels were similar in continent and incontinent transplant patients. Incontinent renal transplant patients recorded a greater daily fluid intake on their 3-day diaries than did continent renal transplant patients. There was no association among renal function as measured by serum creatinine level, incontinence severity, and the effect of incontinence on activities of daily living.

A history of urinary incontinence before renal failure was not predictive of post-transplant incontinence.

This study concluded that urinary incontinence in renal transplant recipients is a prevalent condition that has an impact on activities of daily living and is not predicted by a history of incontinence before renal

failure. Renal transplant recipients may predispose themselves to incontinence with greater fluid intake.

Resiniferatoxin for Interstitial Cystitis

Chen and colleagues[11] conducted a pilot study to assess resiniferatoxin (RTX) for the treatment of interstitial cystitis. This prospective, randomized, double-blind, placebo-controlled study included patients who had received a diagnosis of interstitial cystitis based on the National Institute of Arthritis, Diabetes, Digestive & Kidney Diseases research criteria. After an optional pretreatment intravesical lidocaine wash, 50 mL of a test solution containing placebo, 0.05 μmol/L of RTX, or 0.10 μmol/L of RTX was administered and retained for 30 minutes in the bladder.

Pain was recorded based on a visual analogue scale (VAS). Symptoms were evaluated before treatment and at 4 weeks and 12 weeks posttreatment according to 6 indicators, including VAS for pain, voiding diary, and O'Leary's Interstitial Cystitis Symptom and Problem Indices. Four-week data were available for reporting.

Most patients (14/19) complained of some pain with instillation. However, the majority of subjects were able to complete treatment. There were no clinically meaningful differences between the RTX and placebo groups for any hematologic, biochemical, or cystoscopic parameters. At 4 weeks, 7 of 15 patients in the RTX groups showed improvement in at least 5 of 6 symptom indicators, compared with 1 of 4 patients in the placebo group. This study demonstrated that RTX therapy in patients with interstitial cystitis appears to be safe and well tolerated. Although efficacy results at 4 weeks were promising, they will need to be substantiated with longer follow-up and larger trials.

RTX therapy in patients with interstitial cystitis appears to be safe and well tolerated.

MRI Study of Levator Ani Defects and Obstetric History

Many of the presentations at the AUGS meeting concerned the use of magnetic resonance imaging (MRI) of the pelvic floor. Kearny and colleagues[12] used MRI to examine whether the severity of levator ani defects in primiparous women are independent of their obstetric history. A total of 160 primiparous women 1 year postdelivery and 80 nulliparous women (controls) underwent MRI. The morphology of the levator muscle was studied on each side and classified as normal or abnormal, with subsequent grading of the severity of the defects. Obstetric data were obtained and recorded from the delivery sheet.

Of the parous women, 20% had identifiable defects. Women who had a defect had a second stage of labor that was 1 hour longer, were 3.5 times more likely to have had an operative delivery, were twice as likely to have had an episiotomy, and were 3 times more likely to have sustained an anal sphincter rupture. A major defect was seen in 50% of women who had a forceps delivery, 23% of those who had a vacuum delivery, and 7% of those who had a normal delivery. Other factors that were not statistically significant were gestational age, birth weight, head circumference, oxytocin use, and epidural use.

Although this study clearly demonstrated defects involved in urethral support, some women had defects but were continent and some women were free of defects but incontinent. Thus, the clinical applicability of this study remains unclear.

Conclusion

We encourage urologists with a special interest in urinary incontinence and pelvic prolapse to consider

Main Points

- Data from a study of 210 women with stress urinary incontinence indicate no significant clinical or safety issues when the Uryx urethral bulking agent is compared directly with Contigen.
- Total colpocleisis with levator plication is a vaginal operation for advanced pelvic organ prolapse that has an excellent success rate.
- Duloxetine, a new investigational agent to treat genuine stress incontinence, may also be effective in patients with mixed stress urinary incontinence and overactive bladder.
- A new transdermal form of oxybutynin seems to be as effective as controlled-release tolterodine, with fewer adverse effects.
- Urinary incontinence in renal transplant recipients is a prevalent condition that has an impact on activities of daily living and is not predicted by a history of incontinence before renal failure.

joining and participating in the AUGS. The 2 authors of this review who are urologists (TC and MC) are both members of this society. We believe that awareness of and participation in the AUGS by urologists would build a bridge of understanding and collaboration between these 2 specialties. ■

References

1. Karram MM. Multichannel randomized controlled study to evaluate Uryx® urethral bulking agent in treating female stress urinary incontinence. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
2. Sand PK, Roach MB, Gittelman M, Albrecht D. Sexual function in women with overactive bladder (OAB). Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
3. von Pechmann W, Mutone N, Hale D. Retrospective analysis of total colpocleisis for the treatment of advanced pelvic organ prolapse: a twelve-year experience. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
4. Lukacz ES, Luber KM, Nager CW. Does the tension-free vaginal tape (TVT) system alter voiding? Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
5. Norton PA, Miklos JR, Dmochowski RR, et al, for the Duloxetine SUI Study Group. Mixed stress urinary incontinence (SUI) and overactive bladder (OAB) symptoms: observations on symptom severity and response to duloxetine. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
6. Norton PA, Zinner NR, Yalcin I, Bump RC, for the Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of stress urinary incontinence. *Am J Obstet Gynecol*. 2002;187:40-48.
7. Zinner N, Dmochowski R, Miklos, J, et al. Duloxetine versus placebo in the treatment of stress urinary incontinence (SUI) [abstract]. *Neurourol Urodyn*. 2002;21:383-384.
8. Neimark M, Davila GW, Sanders SW. Effects of transdermal and oral oxybutynin and its metabolites on cystometrogram parameters. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
9. Dmochowski RD, Davila GW, Sanders SW. Randomized, placebo-controlled trial of transdermal oxybutynin vs. tolterodine controlled-release for the treatment of overactive bladder. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
10. Heit M, Natraj N, Blackwell L, et al. The prevalence and severity of urinary incontinence in renal transplant recipients. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
11. Chen TY, Carmel M, Ponsot Y, et al. Preliminary data comparing the safety, tolerance and efficacy of intravesical resiniferatoxin (RTX) in interstitial cystitis. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.
12. Kearney R, Delancy JOL, Chou Q. The severity of defects seen in the levator ani muscle on MR imaging correlate with obstetric history. Presented at: Annual Scientific Meeting of the American Urogynecologic Society; October 17-19, 2002; San Francisco, Calif.